

WHAT IS CLAIMED IS:

1. A crystal of a protein-ligand complex comprising a protein-ligand complex of an N-terminal truncated factor VIII and a ligand, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0 Angstroms; and wherein the N-terminal truncated factor VIII:

- (a) lacks at least 2000 amino acids from the flexible N-terminus of the corresponding full-length factor VIII; and
- (b) retains the C2 domain of the corresponding full-length factor VIII.

10 2. The crystal of claim 1, wherein the ligand comprises a phospholipid.

15 3. The crystal of claim 1, wherein the N-terminal truncated factor VIII comprises an amino acid sequence of amino acids 2174 to 2326 of SEQ ID NO:1, or an amino acid sequence that differs from amino acids 2174 to 2326 of SEQ ID NO:1 by only having conservative substitutions.

4. The crystal of claim 1, wherein the ligand is glycerophosphorylserine.

5. The crystal of claim 1, having space group of P2₁2₁2₁ and a unit cell of dimensions of a=46, b=57, and c=66 Angstroms.

20 6. The crystal of claim 1, wherein the N-terminal truncated factor VIII has secondary structural elements that include an eight-stranded, antiparallel β -barrel arranged in the order: β -sheet (1), β -sheet (2), β -sheet (3), β -sheet (4), β -sheet (5), β -sheet (6), β -sheet (7), β -sheet (8).

25 7. An N-terminal truncated factor VIII lacking from 2000 to 2200 of the first N-terminal amino acids of the corresponding full-length factor VIII.

8. The N-terminal truncated factor VIII of claim 7, comprising an amino acid sequence of amino acids 2174 to 2326 of SEQ ID NO:1, or an amino acid sequence that differs from amino acids 2174 to 2326 of SEQ ID NO:1 by only having conservative substitutions.

9. The N-terminal truncated factor VIII of claim 7, having a selenomethionine that has been substituted for a methionine in said amino acid sequence.

10. The N-terminal truncated factor VIII of claim 7, having an amino acid sequence of amino acids 2169 to 2332 of SEQ ID NO:1, or an amino acid sequence 5 that differs from amino acids 2169 to 2332 of SEQ ID NO:1 by only having conservative substitutions.

11. A method of using the crystal of claim 1 in a drug screening assay, comprising:

(a) selecting a potential ligand by performing structure-based drug design 10 with the three-dimensional structure determined for the crystal, wherein said selecting is performed in conjunction with computer modeling;

(b) contacting the potential ligand with the ligand binding domain of factor VIII; and

(c) detecting the binding of the potential ligand for the ligand binding 15 domain; wherein a potential drug is selected on the basis of its having a greater affinity for the ligand binding domain of factor VIII than that of a standard ligand for the ligand binding domain of factor VIII.

12. The method of claim 11, wherein the standard ligand is glycerophosphorylserine, phosphate or sulfate.

13. A method of using N-terminal truncated factor VIII to grow a 20 crystal of a protein-ligand complex, comprising:

(a) contacting the N-terminal truncated factor VIII with a ligand, wherein the N-terminal truncated factor VIII forms a protein-ligand complex with the ligand; and

(b) growing the crystal of the protein-ligand complex; wherein the crystal 25 effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0 Angstroms.

14. The method of claim 13, wherein said growing is performed by sitting-drop vapor diffusion.

15. The method of claim 13, wherein said ligand is glycerophosphorylserine.